C. REMARKS

The claims have been amended in order to place the application in better form. The fact that the claims have been amended is not to be construed as an admission by Applicants or Applicants' attorneys that such claims, prior to the amendment thereof, are not patentable.

Applicants submit that the present Amendment obviates the rejection of Claims 1, 6-10, 12-15, and 17 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as introducing new matter.

Claims 1, 6, 9, 10, and 17 stand rejected under 35 U.S.C. 102(b) as being anticipated by Hale. This rejection is respectfully traversed.

In the Final Rejection mailed January 29, 2008, from Page 9, line 26 to Page 10, line 10, the Examiner states that the fact that Hale was concerned with a different purpose or does not recognize that the CAMPATH-1H antibody, bound to a synthetic peptide, is effective for reducing an immune response against the antibody and for producing a therapeutic effect by binding to the therapeutic target, does not distinguish the claimed pharmaceutical comprising a therapeutic antibody bound to a peptide that inhibits binding of the antibody to a therapeutic target, from the anti-CD52 humanized antibody, reversibly bound by a CD52 mimotope that inhibits binding of CAMPATH-1H to human lymphocytes expressing CD52. The Examiner also states that Hale discloses the antibody in various buffers, which reasonably can be interpreted as pharmaceutically acceptable carriers. (See also Advisory Action mailed June 18, 2008, Page 3, lines 52-61).

Also, Page 3, lines 61 and 62 of the Advisory Action, the Examiner states that "Applicants' attention is directed to the fact that Claim 9 is not anticipated by Hale."

In the Final Rejection and earlier in the Advisory Action, the Examiner stated that Claims 1, 6, 9, 10, and 17 were rejected under 35 U.S.C. 102(b) as being anticipated by Hale. Clarification is hereby respectfully requested.

Furthermore, Claim 10 depends upon Claim 9, and Claim 17 depends upon Claim 10. Therefore, if Claim 9 is not anticipated by Hale, then Claims 10 and 17 also are not anticipated by Hale.

The present invention, as defined broadly in Claim 1, is directed to a pharmaceutical comprising a therapeutic antibody that binds to a therapeutic target. The antibody has been modified with a peptide that reduces binding of the antibody to the therapeutic target. The modified antibody is effective for reducing side effects caused by the antibody, and produces a therapeutic effect by binding to the therapeutic target. The antibody includes an antibody combining site that binds to the therapeutic target. The peptide is bound to the antibody combining site of the antibody. The pharmaceutical also includes a pharmaceutical carrier.

Hale discloses the testing of the binding of Campath antibodies to various CD52 mimotopes. In the experiments of Hale, however, the Campath antibodies were not modified.

More particularly, Hale discloses various assays, such as ELISA assays and inhibition assays, to determine the binding of unmodified Campath antibodies to various mimotopes of the CD52 epitope to which Campath binds. (See Page 177, column 1, line 21 to Page 178, column 2, line 27) Such assays were conducted in order to

characterize more precisely the epitope which is recognized by Campath antibodies, and to construct analogues of the epitope that would be useful in assays and for purifying unmodified Campath antibodies, as well as for further study of the antibody-antigen binding site.

Figure 8 of Hale (Page 183, column 1) shows that two of the mimotopes tested by Hale inhibited binding of the unmodified Campath antibody to human lymphocytes. Hale, however, does not disclose or even remotely suggest to one of ordinary skill in the art that the Campath antibody may be modified with such mimotopes in order to provide a pharmaceutical comprising a modified antibody as claimed by Applicants.

Hale is directed solely to studying the binding of unmodified Campath antibodies to CD52 mimotopes in order to aid in developing assays and in purifying Campath antibodies, as well as studying the antibody-antigen interaction between Campath antibodies and the CD52 epitope recognized by Campath, or mimotopes thereof.

In contrast to Hale, Applicants modify an antibody with a peptide in order to inhibit binding of the antibody to a therapeutic target, and to reduce side effects caused by the antibody. Although binding of the antibody to a therapeutic target is inhibited, there is some binding of the antibody to the therapeutic target, and a therapeutic effect is produced. Thus, the modified antibody provides a therapeutic effect while side effects caused by the antibody are reduced. Hale does not disclose, nor does Hale even remotely suggest to one of ordinary skill in the art such a modified antibody.

Furthermore, the preamble to Claim 1 defines the present invention as a "pharmaceutical". The Federal Circuit has held that "A preamble to a claim 'has the import that the claim as a whole suggests for it.'" Griffin v. Bertina, 62 U.S.P.Q. 2d 1431

(Fed. Cir. 2002), at 1434, citing Bell Communications Research, Inc. v. Vitalink Communications Corp., 34 U.S.P.Q. 2d 1816 (Fed. Cir. 1995), at 1820. It is clear from reading the specification of the above-identified application that Applicants intended their invention to be a pharmaceutical which causes reduced side effects. Thus, the term "pharmaceutical" provides a further positive limitation to Claim 1 that gives "life and meaning" to the claimed invention. (Corning Glass Works v. Sumitomo Electric U.S.A. Inc., 9 U.S.P.Q. 2d 1962 (Fed. Cir. 1989), at 1966, citing Loctite Corp. v. Ultraseal Ltd., 228 U.S.P.Q. 90 (Fed. Cir. 1985), at 92 and Perkin-Elmer Corp. v. Computervision Corp., 221 U.S.P.Q. 669 (Fed. Cir. 1984), at 675, cert. denied, 469 U.S. 857 (1984), 225 U.S.P.Q. 792; see also Diversitech Corp. v. Century Steps Inc., 7 U.S.P.Q. 2d 1315 (Fed. Cir. 1988), at 1317).

It is clear that Hale does not disclose a pharmaceutical that includes a modified antibody that causes reduced side effects. Instead, Hale discloses a plurality of experimental assays which tested an unmodified CAMPATH-1H antibody. Hale, does not disclose or even remotely suggest to one of ordinary skill in the art that, as a result of such experimentation, one can modify the CAMPATH-1H antibody with a peptide that is bound to the antibody-combining site of the antibody, and employ such antibody in a pharmaceutical, wherein the modified antibody has reduced binding to a therapeutic target and causes reduced side effects. Therefore, Hale does not anticipate Applicants' claimed pharmaceutical nor does Hale render Applicants' claimed pharmaceutical obvious to one of ordinary skill in the art. It is therefore respectfully requested that the rejection under 35 U.S.C. 102(b) be reconsidered and withdrawn.

The claims stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement in that the claims contain subject matter, which does not convey to one skilled in the art that the inventors had possession of the claimed invention. This rejection is respectfully traversed.

The Examiner has taken the position that the written description of the application only reasonably conveys a therapeutic humanized anti-CD52 antibody, Campath-1H, modified by linking two different CD52 mimotopes, in which the antibody-mimotope conjugate reduced the immune response (i.e., cytokine release) and had a therapeutic effect by binding CD52. (See Final Rejection of January 29, 2008, Page 3, line 15 to Page 5, line 10; see also Advisory Action, Page 2, paragraphs 4 and 5).

Contrary to the Examiner's allegations, the specification describes what the invention is as well as what the invention does. The present invention is directed to a pharmaceutical that comprises a therapeutic antibody that includes an antibody combining site, and is modified with a peptide that is bound to the antibody combining site. Those skilled in the art understand readily that different antibodies will have different antibody combining sites, and that the location of the antibody combining site of an antibody can be determined by routine experimentation. Once the antibody combining site has been determined, one can modify the antibody by binding a peptide to the antibody combining site of the antibody by means known to those skilled in the art. In other words, once one skilled in the art has read what the modified antibody includes, one skilled in the art would be able to make the modified antibody by standard techniques known to those skilled in the art. Once the modified antibody is constructed, one skilled in the art would be able to determine through routine experimentation

whether the peptide reduced binding of the antibody to the therapeutic target and reduced side effects caused by the antibody. Therefore, for the above reasons and others, the specification provides a written description of the invention, and it is therefore respectfully requested that the rejection under 35 U.S.C. 112, first paragraph, be reconsidered and withdrawn.

The claims stand rejected under 35 U.S.C. 112, first paragraph, for failing to provide an enabling disclosure. This rejection is respectfully traversed.

The Examiner, from Page 5, line 18 to Page 9, line 6 of the Final Rejection, has held that the specification reasonably does not provide enablement for all modified therapeutic proteins and modified therapeutic antibodies other than CAMPATH-1H modified by linkage to a CD52 mimotope selected from QTSSPSAD and QTSAAAVD. (See also Advisory Action, paragraph bridging Pages 2 and 3).

As noted hereinabove, the Examiner has admitted that the specification is enabling for a pharmaceutical composition comprising Campath-1H modified by linkage to a CD52 mimotope selected from QTSSPSAD and QTSAAAVD. (See Final Rejection of January 29, 2008, Page 5, lines 19-21.)

The Examiner has misunderstood Applicants' previous arguments in that the Examiner believes that such arguments were directed to showing that one skilled in the art would be able to make and test the invention, as opposed to make and use. What Applicants assert is that one skilled in the art would know how to modify antibodies other than Campath-1H in accordance with the present invention. One skilled in the art would be able to determine, by routine experimentation, how to bind peptides to antibody combining sites of other antibodies to provide modified antibodies. Once one

has made a modified antibody, then one can test the modified antibody in order to determine whether binding to the therapeutic target has been reduced. Once one has tested and determined that binding of the modified antibody to the therapeutic target has been reduced, one skilled in the art then would know that such modified antibody can be combined with an appropriate pharmaceutical carrier, and be administered to a mammal to provide a therapeutic effect while reducing side effects, and therefore one skilled in the art is enabled to use the modified antibody. Thus, Applicants have enabled one skilled in the art to make and use the invention, and therefore the claims are patentable under 35 U.S.C. 112, first paragraph.

The Examiner also states that even minor changes in an epitope sequence may affect the antigen binding-function of the antibody. (See Final Rejection, Page 7, lines 9-18; Advisory Action, Page 3, lines 19-35).

Applicants assert that such statement has no relevance with respect to enablement. The mere fact that the amino acid sequence of an epitope has been altered does not mean that an antibody cannot bind to an unmodified epitope. The Examiner appears to be stating that just because an antibody may not be able to bind to a modified epitope, the antibody is not enabled. The possibility that an antibody which binds to a native epitope but does not bind to a modified epitope does not change the fact that the antibody binds to the native epitope, and therefore one skilled in the art is enabled to use the antibody.

The Examiner then states that even one amino acid difference in the peptide used for the modification of the therapeutic antibody could change dramatically the affinity or binding to the antibody combining site.

As noted hereinabove, one skilled in the art can determine whether a modified antibody has reduced binding to the therapeutic target, and whether the modified antibody reduces side effects. If the modified antibody does not have reduced binding to the therapeutic target, and side effects are not reduced, then such modified antibody is not within the scope of the present invention. The mere fact that not every modified antibody is within the scope of the claimed invention does not mean that the present invention is not enabled.

In sum, one skilled in the art can construct a modified antibody having a peptide bound to the antibody combining site of the antibody by means which are known to those skilled in the art. One skilled in the art then can test such modified antibody to determine if binding to the therapeutic target has been reduced, as compared to the unmodified antibody. Once one has determined that the modified antibody has reduced binding to the therapeutic target, one then can combine the modified antibody with a pharmaceutical carrier and administer the modified antibody and the carrier to a mammal to provide a therapeutic effect. Thus, the specification enables one skilled in the art to make modified antibodies which have reduced binding to the therapeutic target, and which provide reduced side effects.

In the rejection, the Examiner has confused the fact that not all modified antibodies are within the scope of the present invention with the legal standard for enablement.

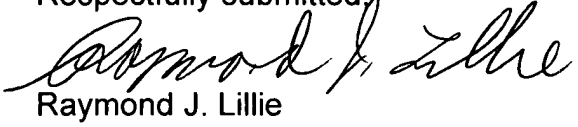
The present invention encompasses only modified antibodies with certain properties. Applicants and only Applicants are the first to have invented an antibody which has been modified with a peptide that reduces binding of the antibody to the

therapeutic target, wherein the peptide is bound to the antibody combining site of the antibody. The modified antibody is effective for reducing side effects caused by the antibody. Such properties can be determined readily by those skilled in the art, and the modified antibodies may be produced by techniques known to those skilled in the art. Thus, one skilled in the art would be able to determine readily whether a particular modified antibody, when combined with a pharmaceutical carrier, infringes the claims of the above-identified application. It would be contrary to the interests of justice to require Applicants to limit the scope of their protection to those modified antibodies which are disclosed specifically, and enable one to avoid infringement by producing a modified antibody which is outside the scope of Applicants' claims yet within the broad scope of Applicants' inventive discovery. Therefore, contrary to the Examiner's allegations, the claimed invention is enabled. It is therefore respectfully requested that the rejection under 35 U.S.C. 112, first paragraph, be reconsidered and withdrawn.

With respect to the obviousness-type double patenting rejection, application Serial No. 09/979,948 issued as U.S. Patent No. 7,465,790 on December 16, 2008. A terminal disclaimer accompanies this Amendment, thereby obviating this rejection.

For the above reasons and others, this application is in condition for allowance, and it is therefore respectfully requested that the rejections be reconsidered and withdrawn and a favorable action is hereby solicited.

Respectfully submitted,



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